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Persistent ALT elevation after 2 years of TDF/TAF-containing ART among persons with HIV/HBV-coinfection: A European multi-cohort collaboration (Euro-B)

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Background

Hepatitis B virus (HBV) infection is a major cause of morbidity and mortality in people living with HIV. We established a multi-cohort collaboration (Euro-B) including HIV/HBV-coinfected participants treated with tenofovir disoproxil fumarate (TDF) and/or tenofovir alafenamide (TAF) from the EuroSIDA Study, the Swiss HIV Cohort Study and the French HIV-HBV cohort.

Objective

To assess factors associated with alanine aminotransferase (ALT) elevation after 2 years of TDF and/or TAF.

Methods

- All participants treated with TDF or TAF with 2 positive HBsAg tests ≥180 days apart and available ALT measurements at treatment start (= baseline) and after 2 years of TDF and/or TAF treatment.
- We assessed the proportion of participants with mild (≥1.25x upper limit of normal (ULN), defined according to the AASLD Guidelines for Treatment of Chronic Hepatitis B 2018) and severe (≥5x ULN) ALT elevation and related risk factors at each time point using descriptive statistics and multivariable logistic regression.

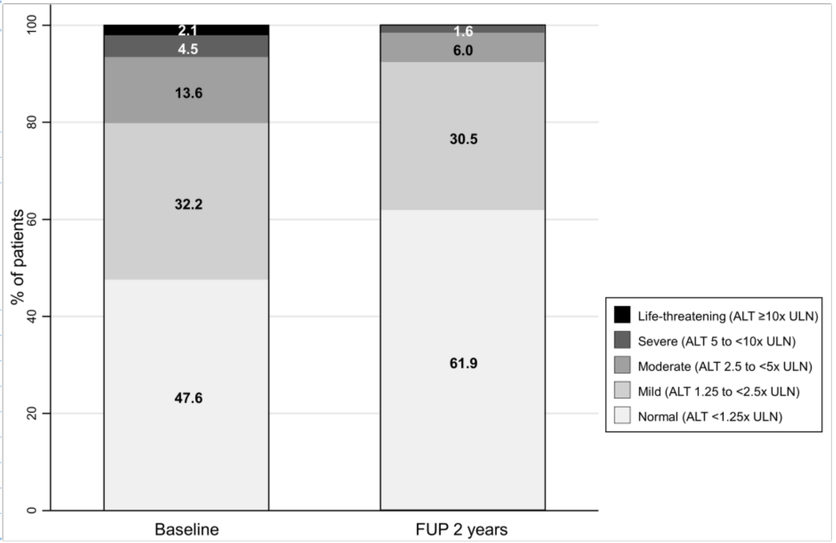
Results

Table 1: Baseline characteristics of Euro-B participants, by ALT level

	Total N=580	ALT <1.25x ULN N=276	ALT ≥1.25x ULN N=304	P-value
Cohort				0.94
Swiss HIV Cohort Study	313/580 (54.0%)	151/276 (54.7%)	162/304 (53.3%)	
EuroSIDA Study	147/580 (25.3%)	69/276 (25.0%)	78/304 (25.7%)	
French HIV-HBV cohort	120/580 (20.7%)	56/276 (20.3%)	64/304 (21.1%)	
Median age [years] (IQR)	41.0 (35.0-47.0)	41.0 (35.0-49.0)	41.0 (36.0-45.5)	0.27
Female sex	110/580 (19.0%)	73/276 (26.4%)	37/304 (12.2%)	<0.001
Mode of HIV transmission				<0.001
men who have sex with men	297/580 (51.2%)	132/276 (47.8%)	165/304 (54.3%)	
heterosexual	148/580 (25.5%)	94/276 (34.1%)	54/304 (17.8%)	
injecting drug use	73/580 (12.6%)	20/276 (7.2%)	53/304 (17.4%)	
unknown or other	62/580 (10.7%)	30/276 (10.9%)	32/304 (10.5%)	
History of liver-related event	27/580 (4.7%)	9/276 (3.3%)	18/304 (5.9%)	0.13
Median BMI [kg/m2] (IQR)	22.7 (20.8-25.3)	22.6 (20.6-25.7)	22.9 (21.1-25.0)	0.50
Ever reported alcohol abuse	128/538 (23.8%)	51/258 (19.8%)	77/280 (27.5%)	0.04
HBV-active NRTI pretreatment	426/580 (73.4%)	194/276 (70.3%)	232/304 (76.3%)	0.10
ART-experienced	365/580 (62.9%)	161/276 (58.3%)	204/304 (67.1%)	0.03
Hepatitis C virus RNA positive	35/533 (6.6%)	7/256 (2.7%)	28/277 (10.1%)	<0.001
Ever anti-HDV positive	61/502 (12.2%)	22/243 (9.1%)	39/259 (15.1%)	0.04
Suppressed HBV VL	120/466 (25.8%)	71/213 (33.3%)	49/253 (19.4%)	<0.001
HBeAg positive	214/410 (52.2%)	72/195 (36.9%)	142/215 (66.0%)	<0.001

Abbreviations: anti-HDV: anti-hepatitis D virus antibodies, ART: antiretroviral therapy, BMI: body mass index, IQR: interquartile range, NRTI: nucleoside reverse transcriptase inhibitors, VL: viral load

Figure: Proportion (%) of participants with ALT elevation at start and after 2 years of tenofovir treatment



ALT elevation categories according to the National Institutes of Health's Division of AIDS grading system

Table 2: Risk factors for ALT elevation (≥1.25x ULN) after 2 years of tenofovir treatment

	Unadjusted OR (95% CI)	P-value	Adjusted* OR (95% CI)	(N=289) P-value
ALT at baseline				
<1.25x ULN	1.0	(ref)	1.0	(ref)
≥1.25x ULN	3.3 (2.3-4.7)	<0.001	2.3 (1.3-4.1)	0.003
Median age	1.0 (1.0-1.0)	0.23		
Female sex	0.7 (0.5-1.2)	0.20		
Mode of HIV transmission				
men who have sex with men	1.0	(ref)		
heterosexual	0.9 (0.6-1.3)	0.46		
injecting drug use	1.7 (1.0-2.8)	0.05		
unknown or other	0.8 (0.4-1.4)	0.39		
Ever reported alcohol abuse	1.5 (1.0-2.3)	0.03	1.4 (0.8-2.5)	0.28
History of liver-related event	1.5 (0.7-3.3)	0.27		
Median BMI at baseline	1.0 (1.0-1.1)	0.66		
Median BMI after 2 years	1.0 (1.0-1.1)	0.81		
HBV-active NRTI pretreatment	1.3 (0.9-2.0)	0.14		
ART-experienced at baseline	1.3 (0.9-1.8)	0.16		
Hepatitis C virus RNA positive	2.6 (1.3-5.2)	0.01	1.6 (0.4-5.8)	0.50
Ever anti-HDV positive	3.4 (2.0-6.0)	<0.001	7.6 (3.1-18.8)	<0.001
Suppressed HBV VL at baseline	0.6 (0.4-0.9)	0.03	0.9 (0.4-1.9)	0.81
Suppressed HBV VL after 2 years	0.6 (0.4-1.0)	0.04	1.1 (0.6-2.2)	0.68
HBeAg positive	2.2 (1.5-3.3)	<0.001	2.3 (1.2-4.7)	0.02

Abbreviations: CI: confidence interval, OR: odds ratio

*All variables with a p<0.1 in univariable analysis were included in the multivariable model. Mode of HIV transmission was excluded due to collinearity

Conclusion

Treatment with TDF or TAF reduces ALT levels in individuals with HIV/HBV-coinfection, but a significant proportion has persistent ALT elevation after 2 years of treatment.

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Declaration of interest :

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